REMARKS

Claims

Claims 1–3, 5–8 and 10–15 are currently under examination with claims 4 and 9 cancelled without prejudice or disclaimer.

Claim amendments

Amended claim 1 recites the material elements (i.e., constituents) of the claimed combination(s). Claim 5 has been amended to recite an independent claim, the support for which can be found in previous claim 1. Claims 10 and 11 are amended to recite the elements of claim 1, to which they are dependent thereon.

Claims 7 and 8 have been amended to correct for a minor typographical error.

It is respectfully submitted that the claim amendments do not raise new matter nor do they impose additional search burden on the Examiner. See, § 1.116(b). Entry thereof is respectfully requested.

Specification

A substitute specification is enclosed herewith. Withdrawal of the objection is respectfully requested.

Claim objections and the rejection under 35 U.S.C. §101/§112

The Examiner is thanked for his careful review of the claims. The objection of claim 10 is moot in view of the amendments.

Applicants disagree with the PTO's contention that the specification fails to provide adequate written description of effector(s) of glutathione metabolism, as recited in present claims 10 and 11. However, in order to facilitate prosecution, the claims have been amended. No agreement is to be implied. It is earnestly submitted that the rejection is moot in view of the amendments.

The rejection of claims 10 and 11 under §112, ¶2, not specifically discussed herein, is moot in view of the amendments. Withdrawal of the rejection is respectfully requested.

Rejection under §103(a)

The Office Action continues to contend that claims 1–3, 5–8 and 10–15 are rendered obvious by Keller (USP 6,262,019) in view of Bisgaard. Bisgaard's reference, which is newly cited, pertains to drug delivery. The rationale for the obviousness rejection is that Keller's

compositions when utilized in a manner (i.e., inhalation) taught by Bisgaard *prima facie* renders obvious the instant claims. Applicants respectfully disagree with this contention.

Keller discloses compositions comprising N-acetyl cysteine (NAC), vitamin C (AA) and a carrier. See, for example, col. 2, lines 42–49 of USP'019. Keller teaches that such compositions are to be administered systemically, preferably orally. See the disclosure bridging lines 26–64 in col. 8 of the patent publication. Keller further teaches that the aforementioned NAC/AA composition can additionally comprise α-lipoic acid, sylmarin, quercitin, l-glutamine, N-acetyl-d-glucosamine or a probiotic. There is no hint or suggestion of compositions *consisting of* α-lipoic acid or a salt thereof and silibinin or a salt thereof as active ingredients, as recited in the present claims.

Applicants respectfully submit that the cited primary reference teaches away from the claimed subject matter. In the paragraphs bridging lines 9–35 of col. 4, Keller explicitly teaches that glutathione depletion is associated with the progression of many diseases and that "the essential element needed by the mammalian cell to manufacture glutathione (GSH) is N-acetylcysteine (NAC)." The reference further teaches that the absorption of N-acetylcysteine (NAC) and transport across the cellular membrane is facilitated by the presence of ascorbic acid (vitamin C). The additional components such as α-lipoic acid, sylmarin, quercitin, l-glutamine, N-acetyl-d-glucosamine or a probiotic are merely used as support ingredients or nutritionals which help maximize the effects of NAC/AA composition. To one skilled in the art, the reference expressly conveys that such antioxidant compositions must contain NAC and Vitamin C as active ingredients and that the other ingredients are merely optional. As such, Keller's compositions are not only different from the compositions claimed herein but teach away from them and indeed are mutually exclusive with them. See, claim 1 and claim 5.

Engeleen discloses that COPD is associated with glutathione deficiency in the lung. The reference is silent as to whether COPD can be treated by administering any of the claimed compounds. Also there is no mention of the instantly claimed route of administration and its effectiveness in treating COPD. A combination of Engeleen and Keller, at most, leads a skilled worker to orally employ Keller's NAC/AA- compositions for the treatment of COPD. However, there is no hint or suggestion of employing a composition consisting of lipoic acid (or a salt thereof) and silibinin (or a salt thereof) in a manner recited in the claims.

Bisgaard is only concerned with possible routes of delivery. There is nothing in Bisgaard's disclosure that would rectify the limitations of Keller or Engeleen (i.e., Bisgaard does not teach or suggest what Keller/Engeleen does not). As such, a combination of Keller and Bisgaard, at most, leads to aerosol compositions comprising NAC and AA. Based on Engeleen's

teachings, the skilled worker may utilize such compositions containing NAC and AA for the treatment of COPD. However, the cited references, even at their broadest interpretation, fail to teach a composition consisting of lipoic acid (or a salt thereof) and silibinin (or a salt thereof) as active ingredients. As such, a combination of Keller and/or Engeleen, further in view of Bisgaard, fails to render obvious the subject matter of the present claims.

With respect to instant claims 2–3 and 13–15, the Office Action contends that the concentration aspects recited in the claims can be optimized through routine experimentation. Applicants respectfully disagree with this contention. Applicants are unsure how the USPTO arrived at this conclusion. As discussed *supra*, Keller is totally silent with respect to an aerosol composition consisting of silibinin and α-lipoic acid (or their salts) as active ingredients. Bisgaard generically teaches that aerosol compositions are useful for delivery of antioxidants; however, the reference is totally silent as to an aerosol formulation consisting of silibinin and α-lipoic acid (or their salts). The Office Action concedes this fact in the last sentence of ¶2 at page 8. In summary, none of the cited references impart any teaching or suggestion that a composition consisting of the claimed doses of silibinin (or a salt thereof) and α-lipoic acid (or a salt thereof) as active ingredients can be effectively formulated and used as an aerosol composition. As such, the references, even at their broadest interpretation, fail to render obvious the subject matter of the present claims. Withdrawal of the rejection is respectfully requested.

Withdrawal of all the rejections and passage to allowance is cordially requested.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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